Design considerations for workflow management systems use in production genomics research and the clinic

AE Ahmed<sup>1,2\*</sup>, JM Allen<sup>3</sup>, T Bhat<sup>3,4,5</sup>, P Burra<sup>3,4†</sup>, CE Fliege<sup>3</sup>, SN Hart<sup>6</sup>, JR Heldenbrand<sup>3</sup>, ME Hudson<sup>3,7</sup>, DD Istanto<sup>7</sup>, MT Kalmbach<sup>8</sup>, GD Kapraun<sup>8</sup>, KI Kendig<sup>3</sup>, MC Kendzior<sup>3</sup>, EW Klee<sup>6</sup>, N Mattson<sup>8</sup>, CA Ross<sup>9</sup>, SM Sharif<sup>2</sup>, R Venkatakrishnan<sup>3</sup>, FM Fadlelmola<sup>1‡</sup>, and LS Mainzer<sup>3,10</sup>

## Supplementary materials

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<sup>&</sup>lt;sup>1</sup>Center for Bioinformatics & Systems Biology, Faculty of Science, University of Khartoum, Sudan <sup>2</sup>Department of Electrical & Electronic Engineering, Faculty of Engineering, University of Khartoum, Sudan

 $<sup>^3</sup>$ National Center for Supercomputing Applications, University of Illinois at Urbana-Champaign, Urbana, IL, USA

<sup>&</sup>lt;sup>4</sup>Department of Computer Science, University of Illinois at Urbana-Champaign, Urbana, IL, USA
<sup>5</sup>Department of Molecular and Cellular Biology, University of Illinois at Urbana-Champaign, Urbana, IL, USA

<sup>&</sup>lt;sup>6</sup>Department of Quantitative Health Sciences, Center for Individualized Medicine, Mayo Clinic, Rochester, MN, USA

<sup>&</sup>lt;sup>7</sup>Department of Crop Sciences, University of Illinois at Urbana-Champaign, Urbana, IL, USA

<sup>8</sup>Department of Information Technology, Department of Laboratory Medicine and Pathology, Mayo

Clinic, Rochester, Minnesota, USA

<sup>&</sup>lt;sup>9</sup>Laboratory Pathology and Extramural Applications, Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA

 $<sup>^{10}</sup>$  Carl R. Woese Institute for Genomic Biology, University of Illinois at Urbana-Champaign, Urbana, IL, USA

<sup>\*</sup>Current address: Bernoulli Institute, University of Groningen, The Netherlands. azzaea@gmail.com

<sup>&</sup>lt;sup>†</sup>Current address: Center for Computational Biology, University of California, Berkeley, CA, USA

<sup>&</sup>lt;sup>‡</sup>These authors equally supervised this work

## 1 Design considerations in building the variant calling pipeline

Design considerations for building a Swift/T-defined Variant Calling pipeline are detailed elsewhere [2], so in this section, we only focus on respecting *Modularity* with an architecture that allows consistent evaluation of Swift/T along with the other 3 WfMSs: Nextflow, CWL and WDL.

In this context, modularity means the ability to construct a complete workflow from a set of smaller and independent processes, apps, CommandLineTools, or tasks/subworkflows (as per the semantics of each WfMS (see section *Methods: Nomenclature*)).

To meet the modularity constraint, src code is arranged as per Fig Supplementary 2a into folders corresponding to each WfMS language, and within which there are folders for calling tasks, unit-testing those tasks, and defining the logic of workflows composed of these tasks (except for Nextflow). The tasks themselves were written in conditionals-free, stand alone bash scripts that provide consistent output definitions and logging functionality regardless of inputs specifications and bioinformatics tools being called (Fig Supplementary 2b). These bash scripts are also free from streaming (i.e., piping) between processes for more robustness and easier debugging of failure source when needed. This further allows seamless switching between Sentieonbased [3] and GATK-based [4, 5] tools (or others) while using the same WfMS (and vice-versa). For easier working with input json files (in case of WDL- and CWL- defined pipelines), helper parser and validator scripts were written in python to populate values from an easy to construct configuration file into the needed input json. This added a layer of abstraction/independence between the processing logic of the workflow (conditions and loops- the DAG definition), and the underlying invocations of the bioinformatics tools. Additionally, it allowed a head-to-head comparison between the 3 languages (See sections Results: Language expressiveness - Results: Support for modularity).

The 4 chosen WfMSs considered here (Nextflow, Swift/T, CWL and WDL) all have engines that adopt the *dataflow*-paradigm. This means an inherent and implicit parallelism in running computations based on data (and resources) availability (rather than location within a script)-making them appropriate for sprouting parallel jobs rather easily (compared with, say, native

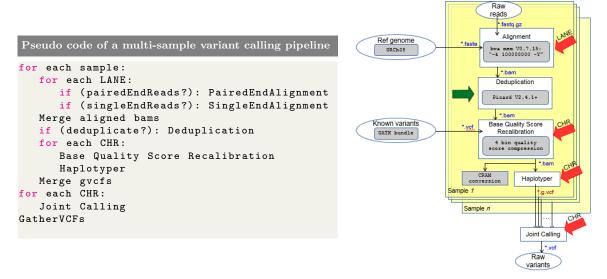
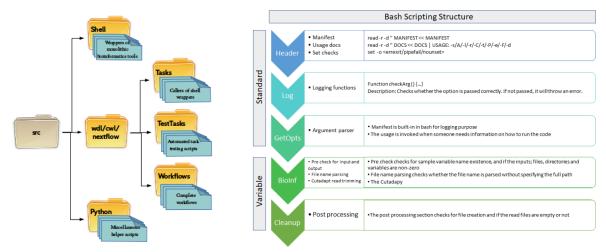


Figure Supplementary 1: Analysis stages in a typical Genome Analysis Toolkit (GATK)-based multi-sample Variant Calling pipeline where each yellow slice is a sample. Gray blocks denote functional equivalence recommendations [1]- with re-alignment (after Deduplication) not shown. Red arrows denote parallel stages, and Green arrows denote optional stages, and thus need a WfMS that supports:Analysis sequential, parallel (looping) and conditional processing and also nesting these within an overall loop.



(a) Code directory structure

(b) Shell script design

Figure Supplementary 2: Architectural code organization of the implemented variant calling pipeline in WDL and Nextflow. A slightly different organization was followed for the Swift/T repo, but it follows similar ideas

bash parallelization and other top-down sequential languages). A complete evaluation of these parallelization and run-time features follows in the main results sections (*Data dependencies and parallelism - Workflow dependency graph resolution and visualization*). Performance aspects are discussed in the remaining results sections (*Executor-level differences - Robustness*). Operational aspects, like debugging and cross-compatibility are examined in the remaining results sections (*Debugging workflows - Cross-compatibility and conformance to standards*).

### 2 Workflows Invocations

# with CWL

```
Custom Nextflow invocation

$ nextflow run workflow.nf -c backend_runtime_and_input.conf

Custom Swift/T invocation

$ swift/t -m backend_name -s runtime_conf.sh workflow.swift

Custom Cromwell invocation

$ # with WDL

$ java -Dconfig.file=backend_and_runtime.conf -jar cromwell.jar run workflow.wdl --
inputs inputs.json --options workflow_options.json
```

Figure Supplementary 3: Typical invocations of workflows written in each language examined in this study, with configuration options specifying the backend against which to run the workflow, its runtime settings and inputs to the workflow run. Example configuration files are provided in our scalability-tst repo.

\$ java -Dconfig.file=backend\_and\_runtime.conf -jar cromwell.jar run workflow.cwl -inputs inputs.yml --type cwl --options workflow\_options.json #The --options
workflow\_options.json directive was not respected in our tests in Jan 2020

# 3 Coding examples

```
Nextflow DSL-1 process

// Defining and using a process (in Tasks/alignment.nf):
SampleNamesChannel = Channel.from(params.SampleName.tokenize(',')) // Comma-separated list of strings input
process Alignment {
   input:
   val SampleName from SampleNamesChannel // Implicit Parallelism over channel elements
   """
   /bin/bash alignment.sh ... # Script in the 'shell' directory
   """
}
```

```
CWL v1.0 CommandLineTool and workflow

# Defining a CommandLineTool (as 'alignmentCommand.cwl'). 'dedupCommand.cwl' is defined similarly:
    cwlVersion: v1.0
    class: CommandLineTool
    baseCommand: alignment.sh # Script in the 'shell' directory
    inputs:
        sampleName:
        type: string
    outputs:
        alignedbam:
        type: File
        outputBinding:
        glob: '*.bam'
```

```
cwlVersion: v1.0
class: Workflow
requirements:
    ScatterFeatureRequirement: {} # For parallelization over input array items
inputs:
    samples_array: String[]
outputs: []
steps:
    alignmentStep:
    run: alignmentCommand.cwl
    scatter: sampleName # Explicit Parallelism over samples
    in:
        sampleName: samples_array
    out: [alignedbam] # Step output
    dedupStep:
    run: dedupCommand.cwl # CommandLineTool definition not provided, but similar to alignmentCommand.cwl above
    scatter: sampleName
    in:
        sampleName: alignmentStep/alignedbam # Implicit dependency via inputs
    out: []
```

```
WDL v1.0 task and workflow

# Defining a task (in Tasks/alignment.wdl):
    version 1.0 #if ommitted, defaults to version "draft-2"
    task alignmentTask {
        input {
            String SampleName
        }
        command {
            /bin/bash alignment.sh ... // Script in the 'shell' directory
        }
    }
}
```

```
version 1.0 #if ommitted, defaults to version "draft-2"
import "Tasks/alignment.wd1" as ALIGN
workflow RunAlignmentTask {
    scatter (sampleName in samples) {
        call ALIGN.alignmentTask as ALIGN_paired  # Task defined with output 'alignedbam'
    call DEDUP.dedupTask as dedup {input: ALIGN_paired.alignedam} # Explicit dependency via inputs
}
}
```

Figure Supplementary 4: Minimal examples demonstrating equivalent parallel and sequential tasks within a variant calling pipeline in each WfMS language. The relative length and sophistication of CWL code can be appreciated here

# 4 Working directory structure

The workflow used here is the 1-step version of the pipeline used for testing scalability. There is a hostname process that is run twice in parallel, then unique hostnames are sorted and collated in a file. Testing was done in a local machine, and relevant comments accompany each workflow run. The complete code can be found in our scalability-tst repo here: https://github.com/azzaea/scalability-tst

#### 4.1 Nextflow

Nextflow defaults to creating a work directory where it is run. Each process will have its own hexa-coded directory of all inputs, outputs, intermediates and logs. No need for a dedicated cat process with Nextflow, since it has efficient channel operators for organizing such outputs.

The output of the workflow is sent to a specific directory in our code. Its contents are shown in the snippet below.

```
Nextflow invocation
$nextflow -version
NEXTFLOW
version 19.10.0 build 5170
created 21-10-2019 15:07 UTC (17:07 CEST)
cite doi:10.1038/nbt.3820
http://nextflow.io
$nextflow run host_process.nf -profile standard --ntasks=2 --log=log.txt
## log omitted
$ cat results.nf/hosts/log.txt
azza-Satellite-P845
$ tree work
  work/
      29
      ___2fd42e9c4edfc45980bd3dac003c9b
            _{\scriptscriptstyle \perp} .command.out
            .command.sh
            _.command.begin
            .command.log
            .command.err
            .command.run
           _.exitcode
      1b
         31200e421cdb1ab2bee26d5460147c
           \_ .command.out
            _{\scriptscriptstyle -} .command.sh
           _.command.begin
           _{-}.command.log
            _.command.err
            .command.run
            _.exitcode
   4 directories, 0 files
```

#### 4.2 WDL: Cromwell

Cromwell defaults to creating a cromwell-execution directory where it is run. Each workflow will have its own directory, and different runs will be different hexa-coded subfolders within. Tasks will further have their own directories nested within their parent sub-workflows or scattering patteren- if present. Similar to Nextflow, each process directory will host all of its inputs, outputs, intermediates and logs.

The output of the workflow is sent to a specific directory via the workflow.options.json file. Its contents are shown in the snippet below.

```
cromwell invocation
$ java -jar $crom --version
cromwell 42
$ java -jar cromwell-42.jar run host_process.wdl --inputs host_process_workflow.json --
    options workflow_options.json
## log omitted, containing final outputs location within cromwell-executions dir before
   they are copied to destination specified within workflow.options.json
$ cat results.cromwell/hosts/log.txt
azza-Satellite-P845
$ tree cromwell-executions
  cromwell-executions/
      f247f741-f15b-4ff7-b661-2b87a9121fd1
         call-catHostsTask
           tmp.246499fd
           execution
             _script.submit
              script
              \_\log.\mathsf{txt}
              _rc
              _stderr
              _stderr.background
              _{	t stdout}
              \_ stdout.background
             _script.background
         call-host1
           shard-1
               tmp.0a8ca919
             \_ execution
                 _script.submit
                 _{-}\mathtt{script}
                 rc
                 stderr
                 _stderr.background
                 \_ stdout
                 _stdout.background
                 _script.background
            shard-0
              tmp.30a11e11
               execution
                 _script.submit
                 script
                 _{
m rc}
```

```
stderr
stderr.background
stdout
stdout.background
script.background
12 directories, 25 files
```

#### 4.3 WDL: toil-wdl-runner

toil-wdl-runner: defaults to deleting the working directory, and does not understand command line arguments acceptable otherwise to Toil. Hence, below we explicitly generate a python equivalent of our WDL code and edit it to accept command line options for specifying a working directory and not deleting it upon successful workflow run.

Additionally, Toil doesn't seem to have the ability to put output files in a user desired destination. Instead, it puts them in the current directory from which it is run. The hostnames retrieved in this case are unusual-preceded by apostrophe or letter (b).

```
Toil invocation
$ toil --version
4.1.0
$ toil-wdl-runner --dev_mode 3 host_process.wdl host_process_workflow.json
## This mode translates our wdl code into python and produces a file named:
   toilwdl_compiled.py
$ sed -i 's/.*getDefaultOptions.*/
                                    parser = Job.Runner.getDefaultArgumentParser()/'
   toilwdl_compiled.py
## To allow passing command line options
$ sed -i 's/.*options.clean.*/
                                 options = parser.parse_args()/' toilwdl_compiled.py
## To prevent deleting the working directory
$ mkdir workDir
$ python toilwdl_compiled.py --workDir workDir --cleanWorkDir never myJobStore
## log omitted, no pointers to where outputs are; but they are placed in this directory
$ cat log.txt
b'azza-Satellite-P845
$ tree workDir
  workDir/
    node-991a1f3e-c498-44af-98a0-ce3b4698291c-2a77c9e44cbe4a17b74b11479a5c5836_
        tmprfhl6a73
           _worker_log.txt
           697be4c6-1294-4982-a484-9408ae2b00fc
             _{
m log.txt}
              tj9id25at
                \_ execution
        tmpv3sjqcun
           _worker_log.txt
           _efe248ad-e14b-466b-9331-225fe59e2e07
        tmpc8ux75re
           worker_log.txt
           62c036a4-5252-413f-b084-61ea8711a532
             _t8hk6ry_n
               __execution
        tmp_2o9cnwe
```

```
worker_log.txt
        569830e3-645c-4749-87d9-a5b017bfaaa4
           tpoe1tau9
            \_ execution
        66b4264f-93fd-4469-acf9-2511b72da37b
        39c81999-e94e-4383-918e-3941352eac67
        16b55c7b-8a47-4725-afed-c35ad581f7e3
        9f67794f-127b-4f22-981f-791e2af310aa
     tmppiv6fdmx
       _worker_log.txt
     tmpab7pga6d
       _worker_log.txt
        f5634d44-86cc-4898-b10e-54b31c48806a
         _{
m telqlwbjb}
            \_ execution
     tmploar_wsi
      __worker_log.txt
25 directories, 8 files
```

#### 4.4 WDL: miniWDL

miniWDL defaults to creating a timestamped named working directory per each workflow run, appended by the workflow name. It requires that only inputs that the workflow actually uses are present in the input json file. Under the hood, for miniWDL to run locally, docker needs to be installed with proper user permissions. A parallelized workflow will consequently be run in <code>Docker swarm</code> mode. This explains the ouput in the example below- hostnames are from this docker swarm environment (not the local environment).

Similar to Toil, miniWDL does not offer the possibility to place outputs in a user defined destination. It doesn't place outputs in the current directory either, but the execution log will direct to their location within the execution directory.

```
miniWDL invocation
$ miniwdl --version
miniwdl v0.7.4
miniwdl.plugin.file_download
                                gs = WDL.runtime.download:gsutil_downloader
    0.7.4
Cromwell 47
$ miniwdl run -i host_process_workflow.json host_process.wdl
## log omitted, containing final outputs location within the timestamped execution
    directory
$ cat /home/azza/github_repos/varCall/scalability-tst/src/wdl/20200604_143731_hostwf/
    output_links/log/log.txt
8ef5b47e1ee3
af718034688c
$ tree 20200604_143731\_hostwf
  20200604_143731_hostwf/
     inputs.json
     outputs.json
     _workflow.log
     call-host1-1
        _task.log
        inputs.json
```

```
outputs.json
     command
     stderr.txt
     stdout.txt
     work
     output_links
  call-catHostsTask
     task.log
     inputs.json
     outputs.json
     command
     stderr.txt
     stdout.txt
     work
      _log.txt
    _output_links
     __result
        log.txt
  wdl
    host_process.wdl
  output_links
   __log
     __log.txt
  call-host1-0
    _task.log
    \_ inputs.json
    _outputs.json
    _{\rm command}
    _stderr.txt
    stdout.txt
    work
    _output_links
16 directories, 26 files
```

### 4.5 CWL: cwltool

cwltool does not create a working directory, and outputs are placed directly in the current directory.

```
cwltool invocation

$ cwltool --version
/home/azza/pythonenvs/toil3/bin/cwltool 3.0.20200324120055

$ cwltool host_process.cwl host_process_workflow.yml
## log omitted, containing final outputs and their locations
$
$ cat /home/azza/github_repos/varCall/scalability-tst/src/cwl/log.txt
azza-Satellite-P845
```

### 4.6 CWL: Cromwell

The general notes of section 4.2 apply here, except that the **-options** directive is not respeced by Cromwell, and hence there is no way to specify the final destination of output files readily.

Instead, the log gives complete path to where outputs are stored within the cromwell-execution directory

```
Cromwell invocation
$ java -jar $crom --version
cromwell 42
$ java -jar $crom run host_process.cwl -i host_process_workflow.yml --type cwl
## log omitted, containing final outputs location within cromwell-executions dir
$ cat /home/azza/github_repos/varCall/scalability-tst/src/cwl/cromwell-executions/
    host_process.cwl/b13c231f-b3aa-4880-b503-afc0edf541e8/call-catsortStep/execution/log
    .txt
azza-Satellite-P845
$ tree cromwell-executions
  cromwell-executions/
   __host_process.cwl
      __b13c231f-b3aa-4880-b503-afc0edf541e8
            call-catsortStep
               inputs
                 _ 1264064947
                  __result.host.txt
                  -532886412
                   \_result.host.txt
               tmp.dd2a99cc
               execution
                 _script.submit
                  glob-b34dfc006a981a93d6da067cf50036fe.list
                 script
                 _{\scriptscriptstyle \perp} log.txt
                 rc
                 _{
m stderr}
                 _stderr.background
                 _log.txt.background
                 _script.background
                  glob-b34dfc006a981a93d6da067cf50036fe
                    _cromwell_glob_control_file
           call-hostStep1
               shard-1
                  tmp.3bf79c99
                  execution
                    _script.submit
                     glob-b34dfc006a981a93d6da067cf50036fe.list
                    _{\mathtt{script}}
                   _rc
                    \_\,\mathtt{stderr}
                    _stderr.background
                    _{	ext{result.host.txt}}
                    result.host.txt.background
                    _script.background
                    glob-b34dfc006a981a93d6da067cf50036fe
                       _cromwell_glob_control_file
               shard-0
               __tmp.1637f792
```

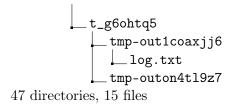
```
execution
               _script.submit
               _glob-b34dfc006a981a93d6da067cf50036fe.list
               _{
m rc}
                _stderr
               _stderr.background
                result.host.txt
                result.host.txt.background
                _script.background
                glob-b34dfc006a981a93d6da067cf50036fe
                 __cromwell_glob_control_file
        call-rangeStep
          _tmp.01de7c14
           execution
            \_ script.submit
            _glob-b34dfc006a981a93d6da067cf50036fe.list
             _{
m script}
            _rc
             stderr
            _stderr.background
            __stdout
            _stdout.background
             _{
m script.background}
             glob-b34dfc006a981a93d6da067cf50036fe
               __cromwell_glob_control_file
22 directories, 42 files
```

#### 4.7 CWL: toil-cwl-runner

The general notes of section 4.3 apply here, except that toil-cwl-runner accepts command line options directly.

```
Toil invocation
$ toil --version
4.1.0
$ mkdir workDir
$ toil-cwl-runner --workDir workDir --cleanWorkDir never host_process.cwl
   host_process_workflow.yml
# log omitted
$ cat log.txt
azza-Satellite-P845
$ tree workDir
  workDir/
   node-89dc310f-9595-4a9e-97aa-f71d3f24652d-2a77c9e44cbe4a17b74b11479a5c5836
      __tmp6s3gi8fm
          _worker_log.txt
          _1a683141-6c14-4ab1-bbc4-b093246bb5bf
              tzxrehcmg
              __out
            _t8syjkal3
```

```
tmp-outsm57wg9r
        tmp-outbmlgcskr
     tah5qtjw0
    _{\rm tnq9ijiwb}
  7c55fea3-7e03-495d-9636-ce8af16bbf80
tmpymlh10pb
__worker_log.txt
tmpi64silti
  _worker_log.txt
 _7222d661-95b0-445b-be5b-a12b83ca1aa8
tmph9k9tuhb
__worker_log.txt
tmpks6eh_0m
__worker_log.txt
tmpzek_gzg3
 _worker_log.txt
 _79905428-016a-4cd1-b968-95cb5bbfa001
     txbku8b2q
    _t2311ba6i
      __out
     _tl4zpjmr7
      __tmp-out2774dp3e
       _tmp-outn66yom55
        result.host.txt
    _{\rm tqix7a77y}
tmpgme2si7h
 _worker_log.txt
 __c9f654f1-5167-422e-b913-e6ff8aa575fb
tmpn38udpjq
  _worker_log.txt
 __d023bfcb-e40e-48bf-af3f-a26b347ae3e0
     ttcurwhla
    _tvjhie4dj
       _tmp-out7a0iq94w
        result.host.txt
       __tmp-outu6c68t67
     t81_96enr
      __out
    _tchmo684i
tmpm0160nc6
 _worker_log.txt
 _54da9631-5317-46f3-8965-4cbb6f842b70
tmp1s19t2nm
  worker_log.txt
 __b2ab1ed4-247a-44ac-82c0-f6ea7584c9a0
     tmphzzn5mh2.tmp
     tmp4c_nsumn.tmp
    tl17es875
     out
    _{
m taqvgxqja}
    _tz_walc91
```



# 5 Scalability results

#### 5.1 On AWS

For the AWS experiments reported below, which were performed in 2019, we used the *then* most recent version of the runners: Cromwell 47 and Nextflow 19.04.1.5072

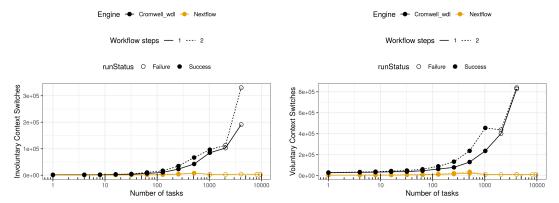


Figure Supplementary 5: (Left) Involuntary and (Right) Voluntary context switches for each scalability scenario.

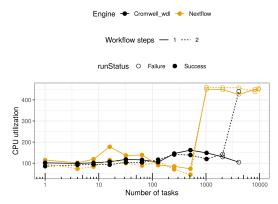


Figure Supplementary 6: CPU utilization on the head node upon the execution of each workflow run.

Cromwell was run with the in-memory database (the default), in run mode. Cromwell uses this database to track the execution of workflows and store outputs. For features like call caching, having a separate mysql database is necessary. This issue may have an effect on the CPU utilization.

#### 5.2 On Biocluster, Recent WfMS versions

The testing reported below was done in 2021, using the most recent version of the runners available: Cromwell 63, Toil 5.3.0 and Nextflow 21.04.1.5556. Experiments were performed on the normal queue of Biocluster, composed of 5 Supermicro SYS-2049U-TR4 nodes, each of 72 cores. The cluster is not dedicated, so the data is affected by the queue load at the time.

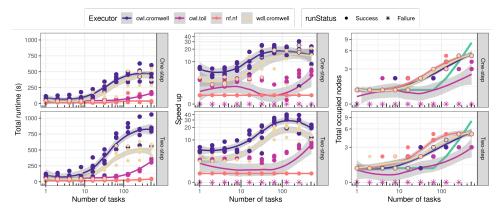


Figure Supplementary 7: Scaling a one-step (top) and two-step (bottom) workflow in Toil+CWL, Cromwell+CWL, Cromwell+WDL and Nextflow. Nextflow can be up to 50x faster than Cromwell, regardless of the language (middle panel), while toil tends to fail unpredictably. The thick green line in rightmost panel is the theoretical number of cluster nodes, which is a ceiling of the ratio of the number of tasks divided by the number of cores per node (72)

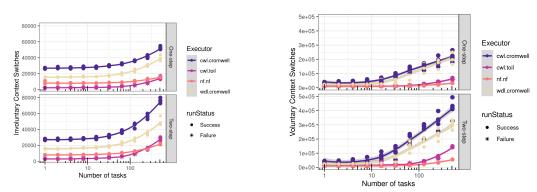


Figure Supplementary 8: (Left) Involuntary and (Right) Voluntary context switches for each scalability scenario

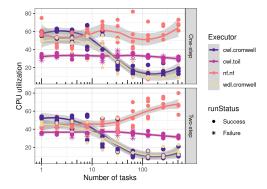
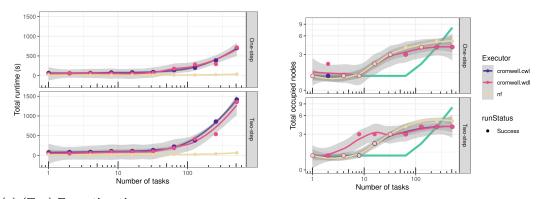


Figure Supplementary 9: CPU utilization on the head node upon the execution of each workflow run

#### 5.3 On Biocluster, Older WfMS versions

The experiments reported below were done in 2019, using the then most recent version of the runners: Cromwell 47 and Nextflow 19.04.1.5072. They were done on the normal queue, composed of 5 Supermicro SYS-2049U-TR4 nodes, each of 72 cores. The cluster is not dedicated, so the data is affected by the queue load at the time.



(a) (Top) Execution times.(Bottom) Nextflow/Cromwell Speed-up.

(b) Tasks distribution across nodes.

Figure Supplementary 10: Scaling a one-step (solid line) and two-step (dashed line) workflow in Cromwell+CWL (black), Cromwell+WDL (yellow) and Nextflow (blue). Nextflow can be up to 20x faster than Cromwell, regardless of the language (Supplementary 10a, bottom). The thick green line in Supplementary 10b is the theoretical number of cluster nodes, which is a ceiling of the ratio of the number of tasks divided by the number of cores per node (72)

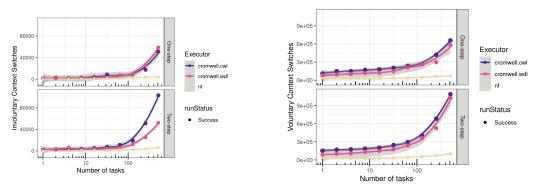


Figure Supplementary 11: (Left) Involuntary and (Right) Voluntary context switches for each scalability scenario

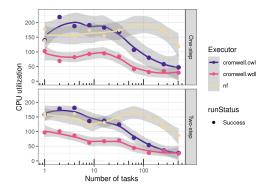


Figure Supplementary 12: CPU utilization on the head node upon the execution of each workflow run

## Acronyms

CWL Common Workflow Languagen.

**DAG** Directed Acyclic Graph.

GATK Genome Analysis Toolkit.

WDL Workflow Description Language.

WfMS Workflow Management System.

### References

- 1. Regier, A. A. *et al.* Functional equivalence of genome sequencing analysis pipelines enables harmonized variant calling across human genetics projects. *Nat. Commun.* **9**, 4038 (2018).
- 2. Ahmed, A. E. *et al.* Managing genomic variant calling workflows with Swift/T. *PloS one* **14** (2019).
- 3. Freed, D. N., Aldana, R., Weber, J. A. & Edwards, J. S. The Sentieon Genomics Tools-A fast and accurate solution to variant calling from next-generation sequence data. *bioRxiv*, 115717 (2017).
- 4. McKenna, A. et al. The Genome Analysis Toolkit: A MapReduce framework for analyzing next-generation DNA sequencing data. Genome Research 20, 1297–1303 (July 2010).
- 5. Van der Auwera, G. A. et al. From FastQ data to high-confidence variant calls: the genome analysis toolkit best practices pipeline. Curr. Protoc. Bioinf. 43, 11–10 (2013).